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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/889,616	05/08/2002	Y. Tom Tang	PF-0662 USN	6963

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EXAMINER	
STEADMAN, DAVID J	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 08/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/889,616	TANG ET AL.	
	Examiner	Art Unit	
	David J Steadman	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,8,15,28 and 29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,8,15,28 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

[1] Claims 1-2, 8, 15, and 28-29 are pending in the application.

[2] Applicants' amendments to the claims, filed July 21, 2004 and August 03, 2004, are acknowledged. The listing of the claims filed August 03, 2004 replaces all prior versions and listings of the claims.

[3] Applicants' amendments to the specification, filed July 21, 2004 and August 03, 2004, are acknowledged.

[4] Applicant's arguments filed July 21, 2004 and August 03, 2004 have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

[5] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Lack of Unity

[6] It is noted that the instant application has been filed under 35 U.S.C. 371. In this case, claim 29 does not have unity of invention with the claims of the elected invention. In accordance with 37 CFR 1.475, unity of invention exists where there is a claimed product, the first claimed method for making the product, and the first claimed method of using the product. 37 CFR 1.475 does not provide for the inclusion of multiple methods of use within the main invention. Therefore, in accordance with 37 CFR 1.475, claim 29

is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Specification/Informalities

[7] In view of the amendment to the specification, the objections to the specification as set forth in items [11]-[12] of the Office action mailed April 21, 2004 are withdrawn.

Claim Objections

[8] Claim 28 is objected to as being grammatically incorrect. It is suggested that applicants amend the claims to recite "and" at the end of part (a) of claim 28.

Claim Rejections - 35 USC § 112, Second Paragraph

[9] In view of the amendment to the claims, the rejection of claim 16 under 35 U.S.C. 112, second paragraph, as set forth in item [13] of the Office action mailed April 21, 2004 is withdrawn.

[10] Claim(s) 15 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

[a] Claim 15 is rejected in the recitation of "effective amount" as one of skill in the art could not determine specific values for the amount based on the disclosure. See *In re Mattison*, 509 F.2d 563, 184 USPQ 484 (CCPA 1975). The phrase "an effective amount" has been held to be indefinite when the claim fails to state the function which is

to be achieved and more than one effect can be implied from the specification or the relevant art. *In re Fredericksen* 213 F.2d 547, 102 USPQ 35 (CCPA 1954).

[b] The method of claim 28 appears to be incomplete as the active step of "detecting the presence of any agonist activity in said sample" (claim 28, part (b)) provides no indication that the compound is being screened for agonist activity of the polypeptide of claim 1. This active step can just as well indicate agonist activity of any other polypeptide that may be present in the sample. Furthermore, there is no indication that the agonist activity is due to the compound itself. It is suggested that applicants clarify the meaning of the claim.

Claim Rejections - 35 USC § 101

[11] The utility rejection of claims 1-2, 8, 15, and 28 under 35 U.S.C. 101 and the corresponding enablement rejection of claims 1-2, 8, 15, and 28 under 35 U.S.C. 112, first paragraph, are maintained for the reasons of record as set forth in items [14] and [15] of the Office action mailed April 21, 2004 and for the reasons stated below.

[12] RESPONSE TO ARGUMENTS: Applicants argue the claims are not drawn to methods of diagnosis, treatment, or prevention and assert the specification provides sufficient guidance regarding therapeutic indications for use of the claimed polypeptide. Applicants argue the specification teaches that NuABP expression is associated with "proliferative, neuronal, inflamed, and cancerous tissues and tissues of the reproductive system" and appears to play a role in reproductive, immune, and neurological disorders, and cell proliferative disorders." Applicants further argue that specific diseases that may

be treated or prevented using the claimed polypeptide are disclosed in the specification. Applicants' argument is not found persuasive.

It is acknowledged that the claims are not drawn to methods of diagnosis, treatment, or prevention. The issue is whether or not the asserted utility of the claimed polypeptide is substantial and specific. The examiner maintains the position that further research is required to use the claimed polypeptide "in the diagnosis, treatment, and prevention of reproductive, immune, and neurological disorders, and cell proliferative disorders including cancer" and as being useful "in the diagnosis, prevention, and treatment of reproductive, immune, and neurological disorders, and cell proliferative disorders including cancer." The specification provides no indication as to how NuABP expression is associated with any "proliferative, neuronal, inflamed, and cancerous tissues and tissues of the reproductive system" or what role the polypeptide "appears to play" in any "reproductive, immune, and neurological disorders, and cell proliferative disorders." Further, while it is acknowledged that specific diseases are disclosed in the specification that can allegedly be treated or prevented by administering the claimed polypeptide, it is noted that this list of diseases is exhaustive and non-specific and the specification provides no specific guidance as to how one of skill in the art can treat or prevent any of the disclosed diseases. In this case, the specification fails to reasonably correlate the biological activity – if any – of the claimed polypeptide to a disease condition. As such, one must determine those diseases – if any – that can be treated or prevented using the claimed polypeptide and must further determine routes of administration, formulations of the polypeptide, and dosages of the polypeptide that can

be used to treat or prevent a disease. As the specification fails to provide this necessary guidance, the claimed polypeptide is not useful in "currently available form."

Applicants argue the specification provides sufficient guidance regarding methods of therapeutic use of the claimed polypeptide. Applicants argue the specification provides sufficient guidance regarding administration of the polypeptide, formulations and preparations, and dosage. Applicants' argument is not found persuasive.

As stated above, the specification fails to provide any specific guidance for treating or preventing any of the disclosed disease states. Further, the general guidance provided in the specification regarding routes of administration and dosage fails to provide the specific guidance that is necessary for treating or preventing a disease state. In this case, further research is required to determine which of those routes of administration and dosage can be used to successfully treat or prevent a disease – if any at all.

Applicants argue the specification provides guidance regarding use of the claimed polypeptides in methods of screening compounds for effectiveness as an agonist or antagonist. Applicants' argument is not found persuasive.

The asserted use of the claimed polypeptide in methods for screening compounds is neither substantial nor specific. This utility is not specific as any polypeptide can be used for screening for agonist and antagonist compounds – this utility applies to the general class of polypeptides. Further, methods for using the claimed polypeptide to identify modulators of its activity also have no substantial utility

as neither the claimed polypeptide nor modulators identified by the claimed methods have a substantial asserted utility.

Claim Rejections - 35 USC § 112, First Paragraph

[13] The written description rejection of claims 1, 8, 15, and 28 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record as set forth in item [16] of the Office action mailed April 21, 2004 and for the reasons stated below.

[14] RESPONSE TO ARGUMENTS: Applicants argue the specification, in addition to the polypeptide of SEQ ID NO:19, describes additional representative species of the genus of claimed polypeptides and discloses methods by which percent identity between amino acid sequences can be determined. Applicants further argue the genus of claimed polypeptides is not widely variant with respect to structure and function as all members of the genus allegedly share structural and/or functional similarities and, as such, the specification describes distinguishing attributes and features of all species of claimed polypeptides. Applicants' argument is not found persuasive.

Contrary to applicants' assertion, the specification discloses only a single representative species of the genus of claimed polypeptides, which encompasses species that are widely variant with respect to both structure and function. Regarding the number of representative species, the specification fails to disclose the structures of any other polypeptide species encompassed by the claimed genus. Instead, the specification "describes" additional members of the genus by percentage identity language, i.e., "90% sequence identity to the amino acid sequence of SEQ ID NO:19" or

fragment language, i.e., a polypeptide fragment comprising at least 30 contiguous amino acids. However, the single representative species of SEQ ID NO:19 fails to represent the genus of claimed variants of SEQ ID NO:19 as recited in parts (b) and (c) of claim 1, particularly in view of the lack of correlation between the structure and function of the species of the claimed genus. In this case, the species encompassed by the genus of polypeptides of claim 1, part (b) can have any function and any structure that is at least 90% identical to SEQ ID NO:19, including any insertions, deletions, additions, and substitutions that fall within the 90% identity limitation. Further, the species encompassed by the genus of polypeptides of claim 1, part (c) can have any function and any structure as long as it comprises at least 30 contiguous amino acids of SEQ ID NO:19. As such, the structures and functions of the polypeptide species encompassed by the genus are widely variant. MPEP § 2163 states that when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. However, the single disclosed species, i.e., SEQ ID NO:19 fails to reflect such variation. Consequently, the genus of claimed polypeptides is not adequately described by the specification.

[15] Even if applicants demonstrate the polypeptide of SEQ ID NO:19 has a specific and substantial or a well-established utility, the scope of enablement rejection of claims 1, 8, 15, and 28 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record as set forth in item [17] of the Office action mailed April 21, 2004 and for the reasons stated below.

[16] RESPONSE TO ARGUMENTS: Applicants argue the full scope of the claimed polypeptides can be made and used without undue experimentation, specifically arguing that the claims are commensurate in scope with the disclosure, the specification provides guidance on how to make and use the claimed invention, the claimed polypeptides share functional similarities, the state of the art demonstrates that making and using the claimed polypeptides is within the scope of routine experimentation, and the amount of experimentation performed by the skilled artisan is routine. Applicants' argument is not found persuasive.

In response to applicants' argument that the claims are commensurate in scope with the disclosure, while it is acknowledged that the specification discloses that the invention encompasses polypeptides "having at least 90% sequence identity to SEQ ID NO:19" and "polypeptide fragments comprising at least 30 contiguous amino acids of SEQ ID NO:19." However, as stated in a previous Office action, the breadth of the claims is not commensurate in scope with the enablement provided by the specification. The polypeptide of claim 1 part (b) broadly encompass any polypeptide having any alterations (substitution(s), insertion(s), deletion(s), and/or addition(s)) within the recited 90% identity limitation and having any function. The polypeptide of claim 1 part (c) encompasses any polypeptide comprising any 30 contiguous amino acids of SEQ ID NO:19 and having any function. However, the specification provides only a single working example of the claimed polypeptide, i.e., SEQ ID NO:19 and fails to provide guidance regarding which of the vast number of polypeptides encompassed by claim 1 would have the biological activity of SEQ ID NO:19.

In response to applicants' argument that the specification provides guidance on how to make and use the full scope of claimed polypeptides, the examiner acknowledges applicants' examples of "how to make" in the specification, however, the specification fails to teach how to make variants of SEQ ID NO:19 that maintain the same biological activity. For example, the specification fails to provide guidance such as those amino acids of SEQ ID NO:19 that are conserved and those that can be replaced without affecting biological activity and fails to teach those amino acids that are involved in DNA binding. Further, the specification fails to provide guidance for using the full scope of claimed polypeptides, which, as stated above, includes polypeptides that do not have the biological activity of SEQ ID NO:19, encompassing polypeptides that have an activity other than that of SEQ ID NO:19 and polypeptides that are non-functional. It is unclear from the specification as to how one would use, for example, a non-functional polypeptide, for screening for modulators, or in the diagnosis, treatment, or prevention of disorders, particularly as the specification fails to enable a skilled artisan to use even SEQ ID NO:19 in the diagnosis, treatment, or prevention of disorders. Thus, the specification fails to provide guidance for making and using the full scope of claimed polypeptides.

In response to applicants' argument that the claimed polypeptides share functional similarities, while it is acknowledged that the specification provides guidance for screening polypeptides for the ability to stimulate transcription, the scope of claimed polypeptides is not limited to those that have the biological activity of SEQ ID NO:19 and instead encompasses polypeptides that have any biological activity, including those

that have no biological activity and the specification fails to provide guidance for making and using polypeptides having any biological activity.

In response to applicants' argument that the state of the art demonstrates that making and using the claimed polypeptides is within the scope of routine experimentation, while it is acknowledged that the specification teaches methods for isolation, the state of the art at the time of the invention acknowledged the high level of unpredictability in altering the amino acid sequence of a polypeptide with an expectation of maintaining the desired biological activity. Such is evidenced by Branden et al. ("Introduction to Protein Structure", Garland Publishing Inc., New York, 1991), who teach "[p]rotein engineers frequently have been surprised by the range of effects caused by single mutations that they hoped would change only one specific and simple property in enzymes" and "[t]he often surprising results of such experiments reveal how little we know about the rules of protein stability... ...they also serve to emphasize how difficult it is to design *de novo* stable proteins with specific functions" (page 247). The teachings of Branden et al. are exemplified by Witkowski et al. (*Biochemistry* 38:11643-11650) who teach that a single amino acid substitution results in conversion of the parent polypeptide's activity from a beta-ketoacyl synthase to a malonyl decarboxylase (see e.g., Table 1, page 11647). As evidenced by these references, there was a high level of unpredictability in the state of the art for altering a protein's sequence at the time of the invention. In view of these references, a skilled artisan would recognize that the amount of experimentation required to make all variants of given polypeptide with an

expectation of maintaining the biological activity of the "parent" polypeptide would not be routine.

In response to applicants' argument that the amount of experimentation performed by the skilled artisan is routine, contrary to applicants' arguments, it is noted that the claimed polypeptides are not limited to those that are human nucleic acid binding proteins. Instead, the claims broadly encompass polypeptides having any biological activity. Even assuming arguendo the scope of polypeptides of parts (b) and (c) of claim 1 were limited to those that have nucleic acid binding activity, the specification would not enable the full scope of these polypeptides as there is a high level of unpredictability in altering a polypeptide sequence with an expectation of maintaining the biological activity of the parent polypeptide as evidenced by Branden et al. and Witkowski et al. Further, the specification fails to provide the necessary guidance for altering the polypeptide of SEQ ID NO:19 with an expectation of maintaining nucleic acid binding activity. While methods of screening polypeptides for those having transcription-activating activity were known in the art at the time of the invention, it was not routine to screen the vast number of polypeptides broadly encompassed by the scope of the claims. In view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, the high level of unpredictability as evidenced by the prior art, and the significant amount of experimentation required to make and use the polypeptides, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention.

Claim Rejections - 35 USC § 102

[17] In view of the amendment to the claims, the rejection of claims 1 and 15 under 35 U.S.C. 102(b) as being anticipated by Sigma Chemical Company 1993 Catalog is withdrawn.

Claim Rejections - 35 USC § 103

[18] In view of the amendment to the claims, the rejection of claim 8 under 35 U.S.C. 103(a) as being unpatentable over Sigma Chemical 1993 Catalog in view of Parish et al. is withdrawn.

Conclusion

[19] Status of the claims:

- Claims 1-2, 8, 15, and 28-29 are pending.
- Claims 1-2, 8, 15, and 28-29 are rejected.
- No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (571) 272-0942. The Examiner can normally be reached Monday-Friday from 7:00 am to 5:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The FAX number for submission of official papers to Group 1600 is (703) 872-9306. Draft or informal FAX communications should be directed to (571) 273-0942. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman, Ph.D.

Patent Examiner
Art Unit 1652

08-13-04